

## Pulsed magnetic field in the treatment of fractures in the elderly: Unraveling mechanisms and optimizing clinical practice

Palmerindo Antônio Tavares de Mendonça Néto <sup>1,\*</sup>, Mayara Magda Dantas Tavares de Mendonça <sup>1</sup>, Carlos Eduardo Miranda <sup>1</sup>, Dirceu Moraes Junior <sup>2</sup>, Carlos Stéfano Hoffmann Brito <sup>3</sup>, Daniel Ramos Gonçalves Lopes <sup>4</sup>, André Câncio de Oliveira Amorim <sup>5</sup> and Paulo Cezar Schutz <sup>6</sup>

<sup>1</sup> Regenera Dor Institute; Juazeiro do Norte, Ce, Brazil.

<sup>2</sup> Clinical Lumius, Joinville, Sc, Brazil.

<sup>3</sup> Carlos Stéfano Institute; Belo Horizonte, Mg, Brazil.

<sup>4</sup> Gaio and Lopes Specialty Medicine; Rio de Janeiro, Rj, Brazil.

<sup>5</sup> Orthopedic Clinical Herculano Silva; Juazeiro do Norte, Ce, Brazil.

<sup>6</sup> Osteoarthritis Clinic, Santa Cruz do Sul; Rio Grande do Sul, Brazil.

World Journal of Advanced Research and Reviews, 2025, 28(02), 093-110

Publication history: Received on 22 September 2025; revised on 27 October 2025; accepted on 30 October 2025

Article DOI: <https://doi.org/10.30574/wjarr.2025.28.2.3689>

### Abstract

This scientific paper explores the use of Pulsed Magnetic Field (PEMF) as a therapeutic modality in the treatment of fractures, with a special focus on its application in elderly patients. It addresses the growing incidence of fractures in the geriatric population, the risk factors that may contraindicate traditional surgical interventions, and the complex physical and biological mechanisms by which PEMF acts to promote bone healing. The detailed analysis of the scientific evidence aims to provide an in-depth understanding of the potential of PEMF as a safe and effective alternative, contributing to the optimization of treatment strategies and improvement of patients' quality of life.

**Keywords:** Fractures; Elderly; Osteoporosis; Pulsed Magnetic Field (PEMF); Alternative Therapies; Quality Of Life.

### 1. Introduction

The treatment of bone fractures represents a constantly evolving field in medicine, with the aim of accelerating healing, reducing pain — minimizing the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics —, reducing postoperative complications, and improving patients' functional outcomes. With the accelerated aging of the world's population, it is estimated that by 2050 there will be more than two billion people aged 60 or over, 426 million of whom will be 80 years of age or older, which implies a significant increase in the incidence of fractures, especially in the elderly. [1.2]

Fractures in this age group are often associated with osteoporosis, sarcopenia, chronic comorbidities, and a higher risk of falls, making the rehabilitation process more complex and prolonged [3]. The loss of functional independence and the increase in post-fracture mortality reinforce the need for less invasive and more effective therapeutic approaches. In this context, non-invasive therapies that favor bone healing and reduce the need for aggressive surgical interventions have gained prominence.

Among these, the Pulsed Electromagnetic Field (PEMF) has emerged as a promising modality, approved by the Food and Drug Administration (FDA) of the United States and recognized by European agencies such as the European Medicines Agency (EMA), through CE certification, for the treatment of fractures with nonunion [4]. Despite the clinical

\* Corresponding author: Palmerindo Antônio Tavares de Mendonça Néto

consolidation of PEMF, its cellular and molecular mechanisms are still the subject of intense investigation. In vitro and in vivo studies demonstrate that PEMF acts at multiple levels, including modulation of ion channels, especially calcium, promoting intracellular influx and activation of signaling pathways such as  $\text{Ca}^{2+}$ /Calmodulin–NO–cGMP [5], in addition to the activation of adenosine A2A receptors, which stimulate cAMP production and promote osteoblastic differentiation [6]. There is also evidence of stimulation of the Wnt/ $\beta$ -catenin, MAPK/ERK, and BMP/TGF- $\beta$  pathways, which are fundamental for osteogenesis and bone remodeling. [7.8]

These mechanisms result in increased cell proliferation, extracellular matrix synthesis, angiogenesis, and reduced local inflammation, favoring bone regeneration. The clinical efficacy of PEMF has been demonstrated in several studies, with consolidation rates between 73% and 85% in nonunion fractures [4], significant improvement in pain, bone function and healing after 8 to 12 weeks of therapy in lower limb fractures [9], and superior results in pain and bone regeneration in cases of osteonecrosis and osteotomies [10]. The global market for PEMF devices is estimated to touch USD 784 million by 2030, with significant growth in North America and Asia Pacific. [11]

Despite the growing evidence and regulatory approval, the efficacy of PEMF in the treatment of fractures, especially in vulnerable populations such as the elderly, still generates debates in the scientific community, raising the question: is the Pulsed Magnetic Field a consolidated therapeutic reality or still a promise in validation? Even with positive results, the heterogeneity in application parameters — such as frequency, intensity, and duration of exposure — still limits clinical standardization [12,13], requiring more controlled and multicenter studies [14,15]. PEMF therefore represents a non-invasive therapeutic approach with significant potential in fracture healing, especially in vulnerable populations such as the elderly. [13.16]

Understanding of biophysical mechanisms [17] and ongoing clinical validation [12,14] are essential for their widespread incorporation into orthopedic practice. This review therefore aims to synthesize the current knowledge about PEMF in the treatment of fractures, detailing its efficacy [16], the epidemiological factors of fractures in the elderly [15], surgical contraindications, and the biophysical mechanisms underlying its action, with the aim of providing a solid basis for evidence-based clinical practice and directing future research in this promising field. [17]

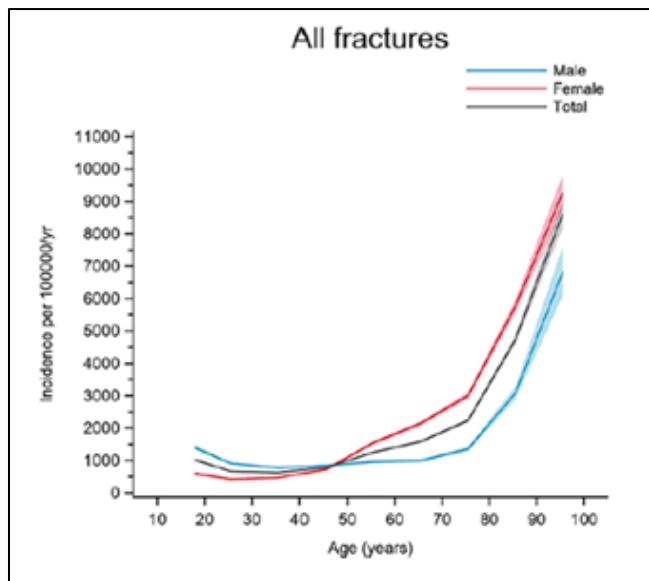
## 2. Incidence of Fractures in the Elderly

The increase in life expectancy of the world population has caused a significant increase in the incidence of fractures among the elderly, configuring a growing challenge for health systems and for the quality of life of affected individuals. Osteoporosis, a condition characterized by low bone mineral density and microstructural deterioration of bone tissue, is one of the main predisposing factors for fractures due to low-energy trauma in this age group [18,19]. It is estimated that one in three women and one in five men over the age of fifty will suffer osteoporotic fractures in their lifetime. [20]

In addition to osteoporosis, changes in gait pattern, balance, and muscle strength due to sarcopenia increase the risk of falls, which are the main precursors of fractures in the elderly [3]. A global systematic review identified that the average prevalence of falls among the elderly is 26.5%, reaching 34.4% in Oceania and 27.9% in the Americas [21]. Among the cases of falls, approximately 19% result in fractures, and 59% occur in the domestic environment, which reinforces the need for preventive strategies aimed at home safety. [22]

Fractures in the elderly have a specific anatomical distribution. Fractures of the lower limbs account for about 47% of cases, followed by upper limbs (32%), ribs and vertebrae (10%), face (8%), and hip (3%) [23]. In 2019, the global incidence of hip fractures in individuals aged 55 years and older was 681.35 per 100,000 population, with projections indicating that this number could double by 2050. [24.25]

The risk of life after a hip fracture is alarming: mortality of 16% to 18% in white women and 5% to 6% in white men is estimated in the first year after the event [26]. By the age of eighty, it is estimated that one in five women will have suffered a hip fracture, and this proportion increases to one in three women by the time they reach the age of ninety [19]. In addition, only 40% of survivors regain the ability to walk independently, and 33% become fully dependent or institutionalized in the year following the fracture. [27]



**Figure 1** Incidence of all fractures in adults in relation to age and gender. There is a significant increase in the incidence of fractures with advancing age, being more pronounced in women, especially after the age of fifty

Risk factors for falls and fractures in the elderly are multifactorial, including advanced age, female gender, osteoporosis, polypharmacy, negative perception of health and vision, difficulty in locomotion, and lack of preventive guidance [28,29]. Early identification of these factors is essential for the implementation of effective prevention and treatment strategies, especially in view of the growing epidemiological and economic burden associated with osteoporotic fractures.

This alarming increase in the incidence of fractures in the elderly and the associated severe consequences make it imperative to seek effective and less invasive therapeutic approaches, such as the Pulsed Magnetic Field, to improve clinical outcomes and quality of life in this vulnerable population.

### 3. Risk Factors That Contraindicate Surgical Treatment in the Elderly

The decision to submit an elderly patient to a surgical intervention for the treatment of fractures is a complex process that requires a careful evaluation of the risks and benefits. Chronological age, by itself, is not the only determinant; Biological age—which reflects functional status, the presence of comorbidities, and physiological reserve—is a much more relevant factor in clinical decision-making [30]. Elderly patients often have a more complex health profile, with multiple preexisting medical conditions that can significantly increase the risk of perioperative complications and mortality, making surgery a less viable option or even contraindicated in certain scenarios. [31]

Among the most critical risk factors are prolonged hospitalization or previous bed riding, which indicate basal debility, and the presence of cardiovascular diseases such as coronary artery disease, recent myocardial infarction, unstable angina, decompensated congestive heart failure, severe valvular heart diseases, and ventricular arrhythmias. These conditions increase the risk of adverse cardiac events during and after surgery [32]. Lung diseases, such as chronic obstructive pulmonary disease (COPD) and asthma, also pose significant risks due to impaired respiratory function, which can be exacerbated by anesthesia and surgical stress. [33]

Other medical conditions that elevate surgical risk include acute renal failure, decompensated diabetes, malnutrition, and frailty syndrome. The latter, characterized by involuntary weight loss, chronic fatigue and low muscle strength, reduces the body's ability to recover from surgical stress, even in minor procedures [34]. The presence of malignant neoplasms also contributes to frailty and worsens the prognosis. Factors such as smoking and high blood pressure, although not absolute contraindications, increase the likelihood of complications [35].

Postoperative complications in the elderly are a major concern. Studies indicate that more than 70% of postoperative deaths occur in this age group, with the main causes being respiratory infections, venous thromboembolism, urinary infections, and loss of muscle mass [31,36]. In addition to physical complications, cognitive impairment is a common and devastating sequela. Postoperative delirium and postoperative cognitive dysfunction (POCD) are conditions that

can lead to loss of independence, depression, and, in severe cases, death. General anesthesia, especially when associated with deep hypnosis, has been correlated with a higher risk of POCD. [34,37]

The time until surgery is also a critical factor. Delays of more than 48 hours after hospital admission are associated with increased mortality and postoperative complications [38].

Given the complexity and risks inherent to surgical intervention in frail older adults with multiple comorbidities, the Pulsed Electromagnetic Field (PEMF) emerges not only as an alternative, but as an essential therapeutic modality to optimize the treatment of fractures, minimizing risks and promoting recovery in a population that often does not qualify for invasive procedures

#### 4. Physical and Biological Mechanisms of the Body's Response to Pulsed Magnetic Field Fracture Treatment

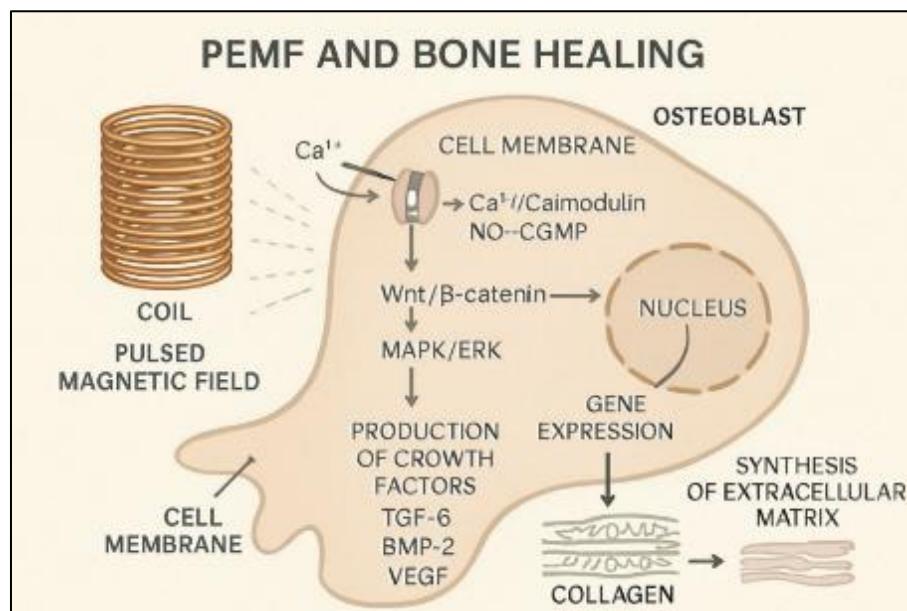
The interaction between low frequency pulsed electromagnetic fields (PEMF) and living tissues represents an advanced manifestation of modern biophysics. Unlike thermal or chemical stimuli, PEMF acts as a non-invasive physical agent, capable of modulating cellular and molecular processes through interaction with the electroactive constituents of biological tissues. These interactions occur by induction of electrical currents in conductive tissues, modulation of transmembrane ionic activity, and activation of mechanosensitive and electrosensitive transduction pathways [7,39,40].

From an electromagnetic point of view, PEMFs operate in frequency ranges between 1 Hz and 100 Hz, with amplitudes of up to a few milliteslas (MT), allowing deep penetration into living tissues due to low resistance to magnetic flux. Faraday's Law of Electromagnetic Induction describes this phenomenon as the generation of electromotive force proportional to the temporal variation of the magnetic flux, expressed by:

$$E = \frac{d\Phi B}{dt}$$

In the differential form, known as the Maxwell–Faraday equation, the relationship between the temporal variation of the magnetic field and the creation of rotational electric fields is described by:

$$\nabla \times \vec{E} = - \frac{\partial \vec{B}}{\partial t}$$



**Figure 2** Molecular and cellular effects of PEMF on regeneration

This electromagnetic induction generates microcurrents in tissues, capable of altering the membrane potential of cells and activating voltage-gated ion channels, especially calcium channels ( $\text{Ca}^{2+}$ ), which trigger the  $\text{Ca}^{2+}/\text{CaM-NO-cGMP}$  biochemical pathway, essential for osteogenesis. [5,7,8,43]

The induced fields present a complex vector topology, with field lines spatially distributed according to the geometry of the tissue, the local conductivity and the configuration of the generating coils [44]. The orientation of magnetic flux density ( $\mathbf{B}$ ) and electric field ( $\vec{E}$ ) vectors relative to membranes, organelles, and surface proteins directly influences the activation of intracellular pathways [45,46]. This interaction can promote changes in membrane polarization, ion channel opening, and activation of cell signaling cascades. [47–49]

At the molecular level, G-protein-coupled membrane receptors, such as adenosine A2A and A3, are particularly sensitive to PEMF. Its activation promotes increased cAMP, activation of protein kinase A (PKA), and inhibition of the nuclear translocation of the NF- $\kappa$ B factor, resulting in a reduction in the expression of inflammatory cytokines such as TNF- $\alpha$  and IL-1 $\beta$  [6,50]. This biochemical modulation favors the proliferation and differentiation of osteoblasts, inhibits osteoclastic activity, and regulates the gene expression of extracellular matrix proteins, such as type II collagen and proteoglycans. In addition, it stimulates the production of growth factors such as TGF- $\beta$ , VEGF, BMP-2/4, and IGF-1, which are essential for bone and cartilage regeneration. [7,50,51]

**Table 1** Growth factors stimulated by PEMF

Factor	Main Function	Effect of PEMF
TGF- $\beta$	Osteoblastic differentiation, collagen synthesis	Increased expression and activity
BMP-2/4	Induction of bone and cartilage formation	Increased gene expression
VEGF	Angiogenesis, vascularization of bone tissue	Increased production
IGF-1	Cellular proliferation and differentiation	Increasing local synthesis
PDGF	Cell proliferation and scarring	Increased clearance

Recent studies demonstrate that PEMF can induce epigenetic modifications in human mesenchymal stem cells, such as the acetylation of histones H3K9ac and H3K27ac in the promoters of osteogenic genes (RUNX2, SP7). These effects are mediated by reactive oxygen species (ROS) and the activation of the p38 MAPK pathway, reinforcing the non-thermal biophysical character of the stimulus and its ability to finely modulate cellular plasticity via intracellular redox sensors. [52]

In addition, mechanosensitive ion channels such as Piezo1, TRP, and L-type calcium channels respond not only to mechanical strains, but also to Lorentz force applied on motile ions in the extracellular space. This force, fundamental for understanding the direct biophysical effect of PEMF on moving electric charges, is expressed by:

$$\vec{F} = q (\vec{v} \times \vec{B})$$

Biological tissues can be modeled as anisotropic and heterogeneous conductors, with variable conductivity according to ionic composition, cell density, and degree of hydration. Computational modeling indicates that, even with magnetic intensities of the order of millitesla, the density of current generated is between  $10^{-3}$  and  $10^{-6}$  A/m<sup>2</sup>, sufficient to influence ion channels without causing direct electrical excitation [53,54]. The distribution of electrical potential in tissues can be described by the anisotropic conduction equation:

$$\nabla \cdot (\sigma \nabla V) = 0$$

Where  $\sigma$  represents the electrical conductivity tensor.

The concept of "bio efficacy window" refers to the existence of a specific range of physical parameters (frequency, amplitude, pulse shape, duration) within which biological effects are maximized. Outside this interval, the effects dissipate or even reverse. Parate et al. (2020) demonstrated, for example, that fields of 1.5 to 2 mT per 10 minutes are ideal for chondrogenic differentiation, while prolonged exposures cancel out this effect. [55]

In the scope of biological physics, pathological states such as fractures or inflammations imply an increase in the local entropy of the biological system. Interventions such as PEMF can be interpreted as organizing forces that restore electrochemical gradients, reduce entropy, and favor homeostasis. This approach is consistent with the thermodynamics of open and self-organized systems, with the free energy of the system represented by:

$$F = U - TS$$

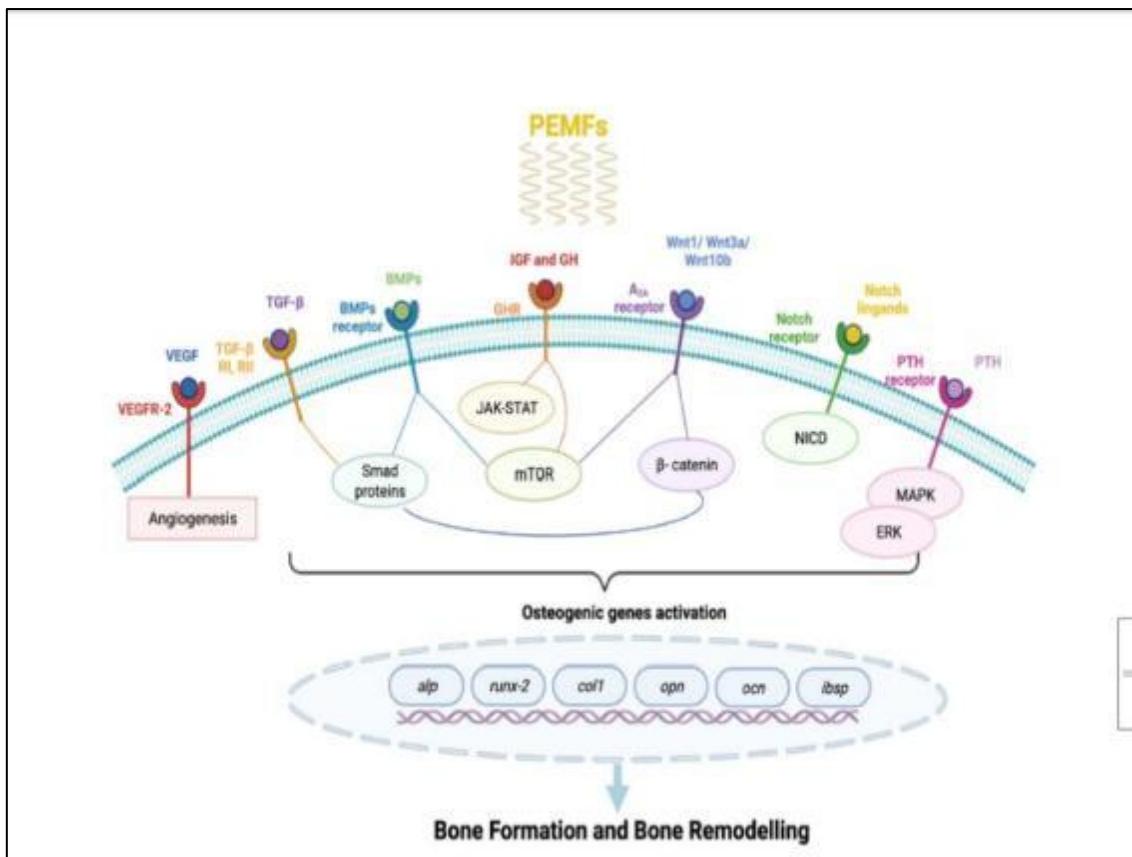
Where F is the free Helmholtz energy, U the internal energy, T the absolute temperature, and S the entropy of the system.

In vivo studies using endochondral ossification models demonstrate that PEMF accelerates chondrogenesis, promotes cartilage removal, and favors the formation of mature bone trabeculae. The expression of mRNA for TGF- $\beta$  and type II collagen increases significantly after exposure to PEMF, indicating a biochemical environment conducive to regeneration [39,56]. In addition, PEMF modulates intracellular signaling pathways such as Wnt/ $\beta$ -catenin (osteoblastic differentiation), MAPK/ERK (cell proliferation), and Notch (mesenchymal cell maturation). [6, 57]

**Table 2** Osteogenesis Markers Modulated by PEMF

Mercader	Function	response to the pelf
ALP (Alkaline Phosphatase)	Bone mineralization	Increased activity
Osteocalcin	Maturation of the bone matrix	Increased expression
Runx-2	Osteoblastic transcription factor	Increased expression
Type 1 collagen	Main component of the bone matrix	Increased synthesis
Osteopenia	Cellular adhesion, mineralization	Increased production

In summary, PEMF acts as a biophysical stimulus capable of inducing synergistic cellular and molecular responses, promoting a pro anabolic environment for bone and cartilage regeneration. By modulating intracellular signaling, extracellular matrix synthesis, and inflammatory response, PEMF accelerates the fracture healing process, offering a promising therapeutic approach, especially in cases where surgical intervention carries high risks or is contraindicated.



**Figure 3** Schematic representation of the cellular and molecular mechanisms by which the Pulsed Magnetic Field (PEMF) influences bone healing. PEMF acts at several levels, from the cell membrane to gene expression, acting in the proliferation and differentiation of osteoblasts and the synthesis of components of the extracellular matrix

## 5. Use of PEMF in Fractures

Pulsed electromagnetic field (PEMF) dosimetry is an essential component in the definition of effective therapeutic protocols for bone healing. Clinical and preclinical studies demonstrate that the intensity, frequency, and duration of PEMF sessions directly influence markers of osteogenesis, such as ALP, osteocalcin, Runx-2, and BMP-2 [57]. Protocols with intensities between approximately 0.1 and 2.8 MT (equivalent to 1–28 Gauss) and frequencies from 10 to 75 Hz are the most used in humans, with evidence of cell activation and acceleration of bone mineralization.

Studies indicate that PEMF induces arteriolar vasodilation in striated muscles of rats, without interfering with systemic blood pressure or tissue temperature. This effect favors local perfusion, optimizing the supply of nutrients and osteogenic factors essential to bone regeneration, in addition to modulating the inflammatory response, creating a biochemical environment favorable to tissue regeneration. Thus, vasodilation induced by PEMF is indicated as a physiological mechanism that contributes to the angiogenic response and the acceleration of healing in fractures that are difficult to consolidate, supporting the clinical application of magnetotherapy in orthopedic contexts. [4.65]

Preclinical trials in rabbits with tibial osteotomy compared 15 Hz PEMF and 1.6 MT peak with combined magnetic fields (CMF) of 76.6 Hz and up to twenty MT, including static field. Exposures ranged between 0.5 and 6 hours per day for 14 to 21 days, revealing a dose-dependent response, with longer duration associated with better biomechanical repair [62]. In a recent study with rats, 4 Hz PEMF was compared to multifrequency packets between 220 and 880 Hz (up to 10 kHz), both with an intensity of ten MT for 1 hour daily for one month. The results indicated superiority of the 4 Hz frequency in bone healing. [41]

**Table 3** Clinical and experimental protocols of PEMF in fractures

Study/Model	Intensity	Frequency	Daily Sessions	Total Duration	Clinical outcomes
Faldini et al. (2024)	2 mT (20G)	75 Hz	8 h/day	90 days	94% union vs. 69% control less pain and necrosis.
Assiotis et al. (2022)	≈2 mT	10 – 50 Hz	8 h/day	≈ 5,6 months	91% healing: union at 3,3 months vs. 4,9 in control
Shi et al. (2013)	ND Orthopulse2	ND	8 h/day	≈ 4,5 months	77,4% healing vs. 48,1% control
Cadossi et al. (2020)	ND	20 Hz	30 min/day	4 weeks	Union from 3 <sup>rd</sup> week; pain reduced from 9 to 1 (VAS)
Sales et al. (2020)	1,6 – 20 mT	15 – 76,6 Hz	0,5 – 6 h/day	14-21 days	Dose-response: more exposure = higher bone strength
Yildiz et al (2023, rat model)	10 mT	4 Hz vs. 220-880 Hz	1 h/day	30 days	4 hz more effective than multifrequency.

Animal models undergoing high-frequency EMPE (HF-PEMF, about four hundred pps) showed significant increase in bone formation after daily 10-minute applications for two weeks [58]. In a clinical context, the commercial Orthopulse II device was used by Shi et al. (2013) in patients with long bone fractures with delayed union, with application of 8 hours per day for approximately 4.5 months, resulting in a union rate of 77.4% compared to 48.1% in the control group.

Assiotis et al. (2022) reported similar results in tibial fractures with delayed union, using approximately two mT fields for 8 hours daily for about 5.6 months. Success was observed in 91% of cases, with a reduction in the average time of marriage from 4.9 to 3.3 months. In proximal femoral fractures (Garden I-III), Faldini et al. (2024) applied two mT PEMF at 75 Hz for 8 hours a day for 90 days, obtaining a consolidation rate of 94% versus 69% in the placebo group, in addition to a lower incidence of osteonecrosis and pain.

**Figure 4** Application of pulsed magnetic field (PEMF) as an adjuvant therapy in the treatment of metatarsal fracture

In addition to randomized controlled trials, several observational studies have documented the efficacy of pulsed electromagnetic field (PEMF) therapy in the treatment of fractures, especially in geriatric populations. In a broad retrospective analysis involving patients with fractures in the nonunion stage, it was observed that the regular use of PEMF resulted in success rates greater than 85%, with radiographic evidence of bone healing and significant pain reduction after eight weeks of treatment [63]. These findings are corroborated by investigations in elderly patients undergoing tibial osteotomies, in which the application of PEMF promoted an increase in bone mineral density and measurable functional improvement, as demonstrated by imaging tests and biochemical markers. [64]

Such evidence reinforces the role of magnetotherapy as an effective therapeutic adjuvant in the recovery of bone integrity, especially in clinical contexts of low osteogenic activity. The case studies in the elderly reinforce the clinical applicability of PEMF in vulnerable populations, with evident benefits in bone healing, pain relief, and functional recovery.

In summary, clinical and preclinical studies demonstrate the significant potential of PEMF in accelerating fracture healing, especially in cases of nonunion and in high-risk populations. Optimizing treatment protocols and overcoming current limitations are crucial for PEMF to reach its full potential as a non-invasive and effective therapy in fracture management.

## 6. Discussion

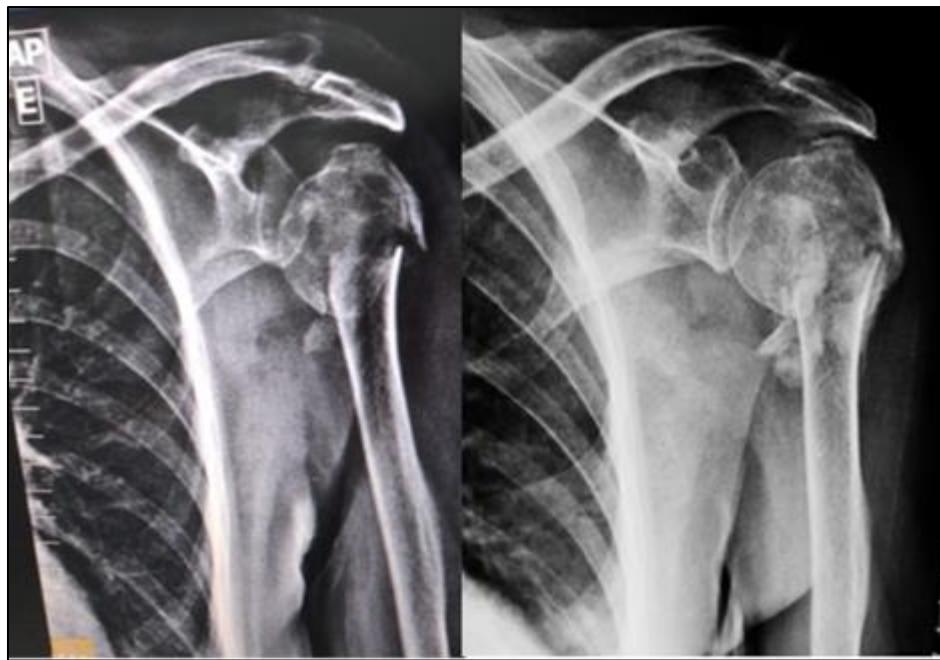
The clinical application of the Pulsed Electromagnetic Field (PEMF) in the elderly has been shown to be a promising therapeutic alternative, especially in view of the limitations imposed by comorbidities and biological fragility that often contraindicate invasive surgical interventions, but the main challenge is to adapt results obtained in the initial studies into effective therapeutic protocols in daily clinical practice.

PEMF, as a non-invasive, painless, and easy-to-apply modality, offers significant benefits in bone healing, pain control and improved quality of life in geriatric patients with fractures.



**Figure 5** Third metatarsal fracture submitted to conservative treatment with immobilization associated with PEMF. With this therapeutic combination, there was a reduction in the need for NSAIDs, in addition to a reduction in the time required to observe radiographic consolidation

In addition to bone healing, PEMF has demonstrated positive effects on cartilaginous regeneration and bone edema reduction and is useful in cases of osteonecrosis and complex fractures.



**Figure 6 and 7** Proximal humeral fracture with anatomical neckline, surgical and large tuberosity. Radiographic evolution in three weeks (and fifteen sessions of PEMF) demonstrating fracture consolidation

In line with the findings of Cadossi et al. (2020), an 83-year-old patient with a proximal humerus fracture and surgical contraindication for congestive heart failure was admitted eight days after the trauma with severe shoulder pain, which was preventing sleep and altering the patient's cognitive status. After clarification about the treatment diagnosis and alignment of expectations, treatment was initiated after signing an informed consent form. The patient was submitted to a therapeutic protocol such as with PEMF (20 Hz, 30 min/day, 560 Gauss for 4 weeks). Progressive radiological consolidation was observed from the third week onwards, with a reduction in pain from 9 to 1 on the VAS scale and functional recovery assessed by LEFS greater than 70%. (Figures 6 and 7)

In addition, PEMF has an indirect analgesic effect by inducing tissue regeneration and accelerating bone healing, which contributes to the reduction of pain in fractures, such as vertebral fractures, and reduces the need for the use of non-steroidal anti-inflammatory drugs (NSAIDs) and opioids. This is especially relevant in elderly patients, in whom opioid use is associated with elevated risks. Studies show that the administration of opioids in this population is related to an increased risk of falls, subsequent fractures, delirium, hyponatremia, and even mortality, with a higher incidence in the first 28 days of use. [66,67,68]

Meta-analyses indicate that long-term exposure to opioids in the elderly can increase the risk of serious falls by up to six times [69], in addition to being associated with adverse effects such as hypogonadism, suppression of the hypothalamic-pituitary-gonadal axis, immunosuppression, paradoxical hyperalgesia, and loss of bone mineral density [70]. Therefore, by promoting pain relief and bone healing in a safe and non-invasive way, PEMF emerges as an effective therapeutic alternative that can contribute to reducing opioid dependence in the elderly, with a positive impact on morbidity, functional recovery, and quality of life. [71]

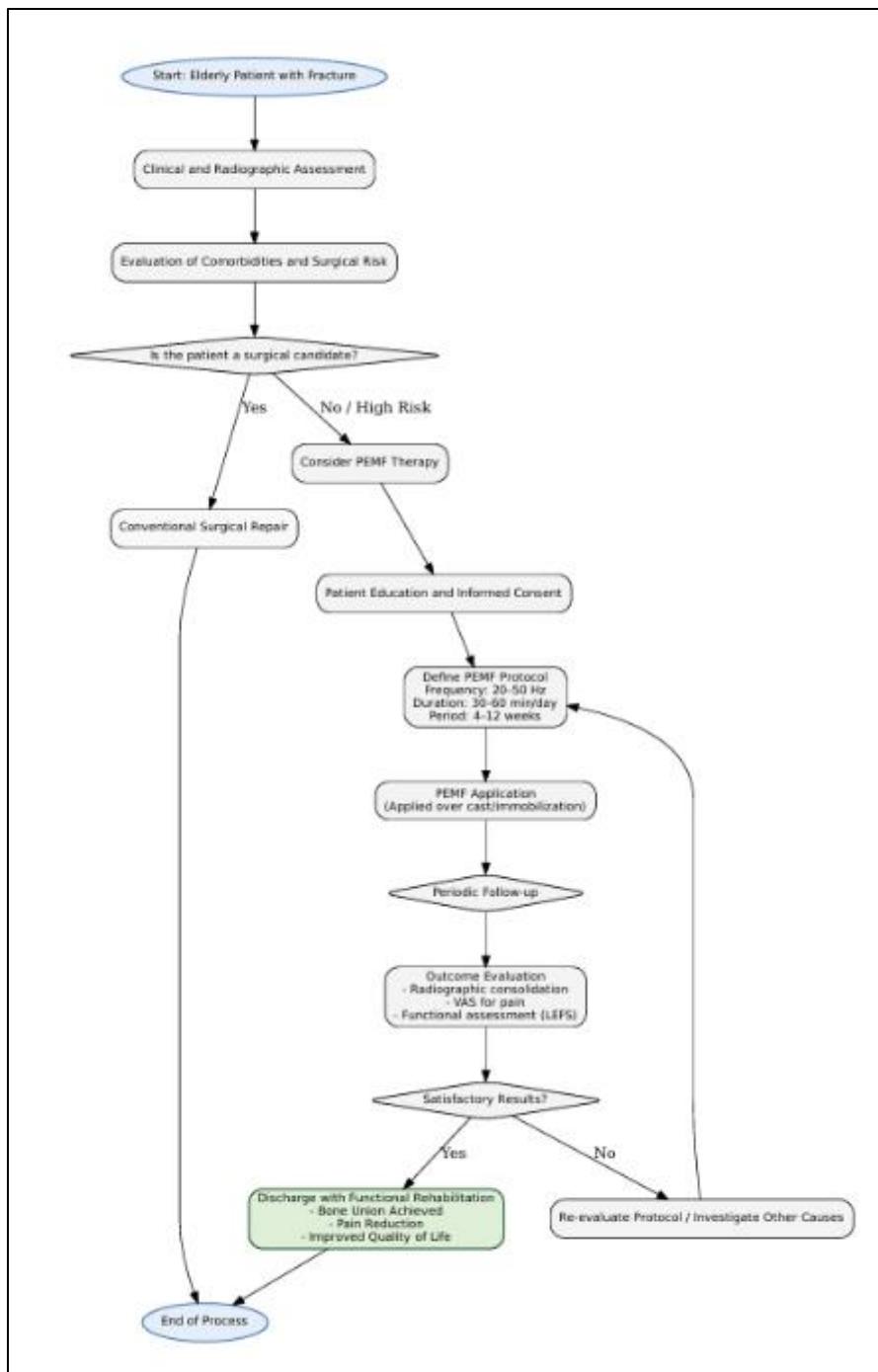


**Figure 8** PEMF is also a therapeutic option in vertebral fractures, with improvement of pain and early return to daily activities

## 7. Conclusion

The Pulsed Electromagnetic Field (PEMF) is an innovative therapeutic modality of high clinical value in the treatment of fractures, especially in a context marked by population aging and the increasing prevalence of osteoporotic fractures in the elderly. Its ability to promote bone regeneration through well-characterized cellular and molecular mechanisms—such as adenosine receptor activation, modulation of extracellular matrix synthesis, and regulation of the inflammatory response—gives PEMF a highly favorable therapeutic profile, especially for patients with multiple comorbidities, in whom conventional surgical interventions present high risks or are contraindicated.

The consolidation of scientific evidence on the biophysical effects of PEMF, together with the advancement of application technologies and the customization of therapeutic protocols, paves the way for its systematic incorporation into clinical guidelines for fracture treatment. Adopting PEMF as a complementary or alternative strategy to surgery can not only accelerate functional recovery and reduce complications but also ease the burden on healthcare systems by promoting safer, more accessible, and patient-centered interventions.



**Figure 9** Flowchart of the Therapeutic Process with PEMF

Despite the promising results, the implementation of the PEMF is not without its challenges. The cost of the devices, the need for strict adherence to prolonged treatment, and the variability in individual patient response represent obstacles to their widespread implementation. In addition, gaps in the literature include the absence of long-term studies assessing the durability of results, direct comparisons with other non-invasive therapies, and the identification of biomarkers that predict treatment response in specific subgroups of patients.

Given its translational potential, the continuity of research — both at the molecular level and in multicenter clinical studies — is essential to refine its applicability, establish optimized dose and frequency parameters, and expand its integration with other therapeutic approaches, such as biomaterials and tissue engineering. The PEMF thus represents not only an effective therapeutic tool, but also an emerging paradigm in regenerative medicine, with profound implications for the orthopedic care of vulnerable populations and for the future of biophysical health therapies.

**Table 4** PEMF-modulated signaling pathways in osteogenesis

Signaling Pathway	Mechanism of Action	Effect on Osteogenesis	Modulation by PEMF
Ca <sup>2+</sup> /Calmodulin-NO-cGMP	Ca <sup>2+</sup> influx » Calmodulin activation » NO production » cGMP increase.	Stimulates osteoblast proliferation and differentiation	↑ Opening of voltage-dependent Ca <sup>2+</sup> channels
Adenosine Receptors A2A/A3	Activation » ↑ cAMP via Gs protein » PKA activation » NF-κβ	Reduces inflammation, promotes osteoblast differentiation	↑ Activation of A2A and A3 receptors
Wnt/β-catenin	β-catenin stabilization » Nuclear translocation » Expression of osteogenic genes	Osteoblast differentiation, bone formation	↑ Stabilization of β-catenin
MAPK/ERK	Kinase cascade » Transcription factor phosphorylation	Cell proliferation, survival	↑ Activation of ERK1/2 pathway
BMP/TGF-β	Receptor binding » Smad phosphor » Gene transcription	Osteoblast differentiation, matrix synthesis	↑ Expression of BMP-2, BMP-4, TGF-β
Notch	Receptor cleavage » Nuclear translocation of NCID	Mesenchymal cell maturation	↑ Modulation of Notch signaling
Ion Channels	Membrane potential alteration » Ion Flux	Cell activation, intracellular	↑ Opening of Ca <sup>2+</sup> , K <sup>+</sup> , Na <sup>+</sup> channels

In summary, PEMF represents an effective and safe therapeutic tool for the treatment of fractures in the elderly, especially in cases of elevated risk for surgery or in situations of compromised bone healing. Its incorporation into clinical practice can contribute to the reduction of morbidity, acceleration of functional recovery, and improvement of quality of life in this vulnerable population.

The application of pulsed electromagnetic field (PEMF) in fractures has a relevant therapeutic role, especially in patients with contraindications to the surgical approach. In addition to offering a non-invasive alternative, PEMF intensifies the biological response to conservative treatments, accelerating bone healing and reducing the time required for immobilization. Its application can be performed directly on immobilization devices, without the need to expose the injured area, which makes this modality especially adaptable to the outpatient and home environment. This synergy with conservative treatment results in additional clinical benefits, promoting early functional recovery with less physiological impact on the patient. [39,65]

**Table 5** Comparative Infographic of Treatments for Fractures in the Elderly

Feature	PEMF Therapy	Surgical Fracture Repair	Pain Management with Opioids
Nature or Treatment	Non-invasive	Highly invasive	Systemic (pharmacological)
Primary Goal	To accelerate bone healing and tissue regeneration.	Mechanical stabilization of the fracture.	Symptomatic pain relief.
Key Advantages	Safe and painless. Reduces swelling and inflammation. Can be used over a cast. Decreases the need for analgesics.	Precise anatomical correction. Allows for early mobilization in some cases.	Effective for intense, acute pain.
Risks & Side effects	Virtually non-existent.	Anesthetic and infection risks.	High risk of falls and subsequent fractures.

	Contraindicated for patients with pacemakers.	Complications in patients with comorbidities. Blood loss.	Delirium, sedation, respiratory depression. Dependence and constipation.
Impact on Quality of Life	Improves functional recovery and independence.	Recovery can be long and painful.	May compromise cognitive status and mobility.
Cost-Effectiveness	Reduces long term hospital and medication costs.	High initial cost (procedure, hospitalization).	Costs associated with managing adverse effects and dependence.
Ideal for Patients...	With high surgical risk, frailty, or non-union fractures.	Who are healthy, with unstable or complex fractures.	With severe, acute pain, under strict, short-term monitoring.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

The authors deny conflicts of interest.

### *Statement of ethical approval*

This study was conducted retrospectively from data obtained for clinical purposes. All data and images were obtained in accordance with the principles of research ethics and in accordance with the 1964 Helsinki Declaration and its later amendments. Informed consent was waived due to the retrospective nature of the study.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

## References

- [1] Ding, Q., Zhou, B., Leung, J., Kwok, T., and Su, Y. (2025). Global trends in burden of fractures, low bone mineral density, and high body mass index. *Osteoporosis International*. <https://doi.org/10.1007/s00198-025-07570-6>
- [2] Cerdex. (2025). Global aging population: Statistics and implications for the future. <https://www.ceradex-sensor.com/articles/global-aging-population-key-statistics-and-trends>
- [3] Migliorini, F., Giorgino, R., Hildebrand, F., et al. (2021). Fragility Fractures: Risk Factors and Management in the Elderly. *Medicina*, 57(10), 1119. <https://doi.org/10.3390/medicina57101119>.
- [4] Vicenti, G., Bizzoca, D., Solarino, G., et al. (2020). The role of biophysical stimulation with PEMFs in fracture healing: From bench to bedside. *Journal of Biological Regulators and Homeostatic Agents*, 34(5 Suppl), 131–135. <https://www.biolifesas.org/EN/Y2020/V34/I5%28S1%29/131>
- [5] Cristiano, L., and Pratellesi, T. (2020). Mechanisms of Action and Effects of Pulsed Electromagnetic Fields (PEMF) in Medicine. *Journal of Medical Research and Surgery*, 1(6), 1–4. <https://doi.org/10.52916/jmrs204033>
- [6] Kaadan, A., Salati, S., Setti, S., and Aaron, R. (2024). Augmentation of deficient bone healing by pulsed electromagnetic fields. *Bioengineering*, 11(12), 1223. <https://doi.org/10.3390/bioengineering11121223>
- [7] Wang, A., Ma, X., Bian, J., et al. (2024). Signalling pathways underlying pulsed electromagnetic fields in bone repair. *Frontiers in Bioengineering and Biotechnology*, 12, 1333566. <https://doi.org/10.3389/fbioe.2024.1333566>
- [8] Yuan, J., Xin, F., and Jiang, W. (2018). Underlying signaling pathways and therapeutic applications of PEMFs in bone repair. *Cellular Physiology and Biochemistry*, 46(4), 1581–1594. <https://doi.org/10.1159/000489206>
- [9] Gajjar, B., Bhavsar, N., Shah, N., Shah, K., and Patel, P. (2024). Effect of Low Frequency PEMF Therapy on Bone Healing and Quality of Life. *International Journal of Health Sciences and Research*, 14(1), 28. <https://doi.org/10.52403/ijhsr.20240128>

[10] Fontanesi, G., Setti, S., and Traina, G. (2020). Pulsed electromagnetic fields in orthopaedics: From bench to bedside. *Clinical Cases in Mineral and Bone Metabolism*, 17(2), 101–106. <https://doi.org/10.11138/ccmbm/2020.17.2.101>

[11] Grand View Research. (2024). Pulse Electromagnetic Field Therapy Devices Market Report, 2030. <https://www.grandviewresearch.com/industry-analysis/pulse-electromagnetic-field-pemf-therapy-devices-market-report>

[12] Raposo, H. (2024). The scientification of the clinic and the standardization of medical practices: on the role of professional judgments in the world of evidence. *Health and Society*, 33(4). <https://www.scielosp.org/article/sausoc/2024.v33n4/e230181pt/pt/>

[13] Pinas, W. G. C. (2002). Effect of the electromagnetic pulse field on bone repair processes [Master's thesis, Federal University of São Paulo]. Repository UNIFESP. <https://repositorio.unifesp.br/handle/11600/18028>

[14] Sukekava, F., et al. (2008). Multicenter clinical trials: a literature review. *Periodontics*, 18(1), 26–30. <https://pesquisa.bvsalud.org/portal/resource/pt/lil-544188>

[15] Ribeiro, A. C. K. (2012). More effective physiotherapeutic interventions in postoperative rehabilitation in elderly people with femoral fractures [Final paper, Universidade Federal de Minas Gerais]. Repository UFMG. <https://repositorio.ufmg.br/handle/1843/43606>

[16] Rocha, P. L. D. (2016). The use of pulsed electromagnetic fields (PEMF) in the treatment of pseudoarthrosis [Final paper, Catholic University of Brasilia]. Repository UCB. <https://repositorio.ucb.br:9443/jspui/handle/123456789/11844>

[17] DNA Reverse. (2023). Electromagnetic fields with pulsed frequencies: biophysical mechanisms and clinical applications. <https://dnareverse.com.br/campos-eletromagneticos-com-frequencias-pulsadas/>

[18] Li, G., Thabane, L., Papaioannou, A., et al. (2017). An overview of osteoporosis and frailty in the elderly. *BMC Musculoskeletal Disorders*, 18, 46. <https://doi.org/10.1186/s12891-017-1403-x>

[19] Kanis, J. A., et al. (2021). SCOPE 2021: A new scorecard for osteoporosis in Europe. *Archives of Osteoporosis*, 16(1), 82. <https://doi.org/10.1007/s11657-021-00994-8>

[20] International Osteoporosis Foundation. (2024). Epidemiology of osteoporosis and fragility fractures. <https://www.osteoporosis.foundation/facts-statistics/epidemiology-of-osteoporosis-and-fragility-fractures>

[21] Salari, N., Darvishi, N., Ahmadipanah, M., et al. (2022). Global prevalence of falls in the older adults: a systematic review and meta-analysis. *Journal of Orthopaedic Surgery and Research*, 17, 173. <https://doi.org/10.1186/s13018-022-03222-1>

[22] World Health Organization. (2024). Fragility fractures: Fact sheet. <https://www.who.int/news-room/fact-sheets/detail/fragility-fractures>

[23] James, S. L., et al. (2020). The global burden of falls: estimates from the Global Burden of Disease Study 2017. *Injury Prevention*, 26(Suppl 2), i3–i11. <https://doi.org/10.1136/injuryprev-2019-043286>

[24] Feng, J.-N., Zhang, C.-G., Li, B.-H., et al. (2023). Global burden of hip fracture: The Global Burden of Disease Study. *Osteoporosis International*, 35, 41–52. <https://doi.org/10.1007/s00198-023-06907-3>

[25] Ebeling, P. R. (2023). Hip fractures and aging: A global problem requiring coordinated global solutions. *Journal of Bone and Mineral Research*, 38(8), 1062–1063. <https://doi.org/10.1002/jbmr.4881>

[26] Selçuk, E. (2025). Beyond the fracture: Mortality risk and survival after hip fractures in the elderly. Intech Open. <https://doi.org/10.5772/intechopen.1010851>

[27] Cooper, C., Atkinson, E. J., Jacobsen, S. J., O'Fallon, W. M., and Melton, L. J., 3º (1993). Population-based study of survival after osteoporotic fractures. *American Journal of Epidemiology*, 137(9), 1001–1005. <https://doi.org/10.1093/oxfordjournals.aje.a116756>

[28] Rizzoli, R., et al. (2014). Management of osteoporosis of the oldest old. *Osteoporosis International*, 25(11), 2507–2529. <https://doi.org/10.1007/s00198-014-2784-9>

[29] Praveen, A. D., Aspelund, T., Ferguson, S. J., et al. (2024). Refracture and mortality risk in the elderly with osteoporotic fractures: The AGES-Reykjavik study. *Osteoporosis International*, 35, 1231–1241. <https://doi.org/10.1007/s00198-024-07096-3>

[30] Zhou, Y., Zhang, Y., Lu, P., et al. (2022). Treatment strategies for non-displaced femoral neck fractures in the elderly. *Arthroplasty*, 4, Article 8. <https://doi.org/10.1186/s42836-022-00111-0>

[31] Zhang, H., Ma, L., and Yu, X. (2025). Risk factors of postoperative complications and in-hospital mortality after hip fracture among patients older than 80 years old: A retrospective study. *BMC Surgery*, 25, Article 122. <https://doi.org/10.1186/s12893-025-02862-4>

[32] American Academy of Orthopaedic Surgeons. (2021). Management of Hip Fractures in Older Adults: Clinical Practice Guideline. <https://www.aaos.org/hipfxcpg>

[33] Chen, X., Huang, Y., Lin, D., et al. (2025). The incidence and risk factors of perioperative delirium in elderly patients with hip fracture. *Journal of Orthopaedic Surgery and Research*, 20, Article 114. <https://doi.org/10.1186/s13018-025-06114-2>

[34] Qi, Y., Li, Y., Zou, J., et al. (2022). Risk factors for postoperative delirium in geriatric patients with hip fracture: A systematic review and meta-analysis. *Frontiers in Aging Neuroscience*, 14, 960364. <https://doi.org/10.3389/fnagi.2022.960364>

[35] Wan, W., Li, L., Zou, Z., and Chen, W. (2025). Predictive model of delirium risk after surgery for elderly hip fractures: A meta-analysis. *European Geriatric Medicine*, 16, 245–270. <https://doi.org/10.1007/s41999-024-01095-7>

[36] Barbosa, T. d. A., Souza, A. M. F. d., Leme, F. C. O., Grassi, L. D. V., Cintra, F. B., Lima, R. M. e, Gumieiro, D. N., Lima, L. H. N. e. (2019). Perioperative complications and mortality in elderly patients undergoing surgery for femoral fractures. *Brazilian Journal of Anesthesiology*, 69(6), 561–567. <https://doi.org/10.1016/j.bjane.2019.10.008>

[37] Wang, C., Tan, B., and Qian, Q. (2023). Impact of perioperative enhanced recovery nursing model on postoperative delirium in elderly patients with femoral neck fractures. *BMC Musculoskeletal Disorders*, 24, Article 947. <https://doi.org/10.1186/s12891-023-07068-4>

[38] Tang, W., Wang, Y., He, Y., et al. (2025). Effect of early rehabilitation on hospital stay and postoperative complications in elderly hip fracture patients: A prospective cohort study. *Journal of Orthopaedic Surgery and Research*, 20, Article 84. <https://doi.org/10.1186/s13018-024-05354-y>

[39] Cadossi, R., Massari, L., Racine-Avila, J., and Aaron, R. K. (2020). Pulsed electromagnetic field stimulation of bone healing and joint preservation: Cellular mechanisms of skeletal response. *JAAOS Global Research and Reviews*, 4, e19.00155. <https://doi.org/10.5435/JAAOSGlobal-D-19-00155>

[40] Hu, H. et al. Promising application of Pulsed Electromagnetic Fields (PEMFs) in musculoskeletal disorders. *Biomedicine and Pharmacotherapy*, v. 131, p. 110767, 2020. DOI: 10.1016/j.biopha.2020.110767.

[41] Akdag, M. Z. et al. Effect of 4 Hz and multifrequency pulsed electromagnetic field (PEMF) on bone fracture healing. *Biotechnology and Biotechnological Equipment*, v. 38, n. 1, p. 2385415, 2024. DOI: 10.1080/13102818.2024.2385415.

[42] Leonardo, P. S. et al. Applications of Pulsed Electromagnetic Field Therapy in Skeletal-Muscle System: An Integrative Review. *Manual Therapy, Posturology and Rehabilitation Journal*, v. 21, p. 1252, 2023. DOI: 10.17784/mtprehabjournal.2023.21.1252.

[43] Varani, K. et al. Pulsed Electromagnetic Field Stimulation in Osteogenesis and Chondrogenesis: Signaling Pathways and Therapeutic Implications. *International Journal of Molecular Sciences*, v. 22, n. 2, p. 809, 2021. DOI: 10.3390/ijms22020809.

[44] Rahbek, U. L. et al. Biological effects of pulsed electromagnetic field stimulation on bone healing: a review. *Bioelectromagnetics*, v. 26, n. 2, p. 88–98, 2005. DOI: 10.1002/bem.20094.

[45] Leronni, A. et al. On the coupling of mechanics with bioelectricity and its role in morphogenesis. *Journal of the Royal Society Interface*, v. 17, 2020. DOI: 10.1098/rsif.2020.0177.

[46] Nunn, A. V. W.; GUY, G. W.; BELL, J. D. Bioelectric Fields at the Beginnings of Life. *Bioelectricity*, v. 4, n. 4, p. 237–248, 2022. DOI: 10.1089/bioe.2022.0012.

[47] Feng, W. A Theoretical Derivation of Faraday's Second Law of Electromagnetic Induction. *International Journal of Physics*, v. 8, n. 4, p. 120–123, 2020. DOI: 10.12691/ijp-8-4-1.

[48] McCloskey, J. Fundamentals of Electromagnetics, Magnetic Field, Current, and Inductance. NASA Technical Reports Server, 2024. DOI: 10.31219/osf.io/7xgqv.

[49] Tota, M., Jonderko, L., Witek, J., et al. (2024). Cellular and molecular effects of magnetic fields. *International Journal of Molecular Sciences*, 25(16), 8973. <https://doi.org/10.3390/ijms25168973>

[50] Caliogna, L., Medetti, M., Bina, V., et al. (2021). Pulsed electromagnetic fields in bone healing: Molecular pathways and clinical applications. *International Journal of Molecular Sciences*, 22(14), 7403. <https://doi.org/10.3390/ijms22147403>

[51] 55. Kim, J., et al. (2006). PEMF induces VEGF production and osteoblast proliferation. *Bioelectromagnetics*, 27(7), 503–511. <https://doi.org/10.1002/bem.20245>

[52] CHIARAMELLO, E. et al. Cell transmembrane potential in contactless permeabilization by time-varying magnetic fields. *Computers in Biology and Medicine*, v. 135, 104587, 2021. DOI: 10.1016/j.combiomed.2021.104587

[53] BERNARDI, P.; D'INZE, G. Physical mechanisms for electromagnetic interaction with biological systems. In: *Electromagnetic Interaction with Biological Systems*. Springer, 1989. DOI: 10.1007/978-1-4684-8059-7\_9

[54] CASTELLO, P.; JIMENEZ, P.; MARTINO, C. F. The Role of Pulsed Electromagnetic Fields on the Radical Pair Mechanism. *Bioelectromagnetics*, 2021. DOI: 10.1002/bem.22358

[55] PARATE, D. et al. Pulsed electromagnetic field stimulation of mesenchymal stem cells for cartilage repair. *Stem Cell Research and Therapy*, v. 11, n. 1, 2020. DOI: 10.1186/s13287-020-1566-5

[56] Zhou, J., et al. (2019). Effects of PEMF on bone marrow mesenchymal stem cells: proliferation and osteogenic differentiation. *Cellular Physiology and Biochemistry*, 52(1), 123–135. <https://doi.org/10.1159/000495123>

[57] Pettersen, R. D., et al. (2021). PEMF stimulation improves osteoblast survival and collagen production. *Journal of Orthopaedic Research*, 39(2), 345–352. <https://doi.org/10.1002/jor.24876>

[58] Zhao, Z., Li, X., Wang, L., et al. (2021). Pulsed Electromagnetic Fields in Bone Healing: Molecular Pathways and Clinical Applications. *Frontiers in Bioengineering and Biotechnology*, 9, 8303968. <https://doi.org/10.3389/fbioe.2021.8303968>

[59] Zhao, Z., Li, X., Wang, L., et al. (2019). Enhancement of bone consolidation using high-frequency pulsed electromagnetic fields (HF-PEMFs): An experimental study on rats. *Bioelectromagnetics*, 40(5), 345–354. <https://doi.org/10.1002/bem.22202>

[60] Shi, H. F., Xiong, J., Chen, Y. X., et al. (2013). Early application of pulsed electromagnetic field in the treatment of postoperative delayed union of long-bone fractures: a prospective randomized controlled study. *BMC Musculoskeletal Disorders*, 14, 35. <https://doi.org/10.1186/1471-2474-14-35>

[61] Assiotis, A., Sachinis, N. P., Chalidis, B. E. (2022). Pulsed electromagnetic fields for the treatment of tibial delayed unions and nonunions. *Journal of Orthopaedic Surgery and Research*, 7(1), 1–7. <https://doi.org/10.1186/s13018-022-02845-2>

[62] Faldini, C., et al. (2024). Pulsed Electromagnetic Field Stimulation in Bone Healing and Joint Preservation: A Narrative Review of the Literature. *Applied Sciences*, 14(5), 1789. <https://doi.org/10.3390/app14051789>

[63] Zhao, Z., Li, X., Wang, L., et al. (2020). The Effect of Pulsed Electromagnetic Field and Combined Magnetic Field Exposure Time on Healing of a Rabbit Tibial Osteotomy. *Bioelectromagnetics*, 41(2), 123–132. <https://doi.org/10.1002/bem.22245>

[64] Murray, H. B., and Pethica, B. A. (2016). A follow-up study of the in-practice results of pulsed electromagnetic field therapy in the management of nonunion fractures. *Orthopedic Research and Reviews*, 8, 67–73. <https://doi.org/10.2147/ORR.S113756>

[65] Ziegler, P., Böhme, J., Sehmisch, S., and Stürmer, K. M. (2019). Pulsed electromagnetic field therapy improves osseous consolidation after high tibial osteotomy in elderly patients. *Journal of Clinical Medicine*, 8(11), 2008. <https://doi.org/10.3390/jcm8112008>

[66] Ehnert, S., Schröter, S., Aspera-Werz, R. H., et al. (2019). Translational insights into extremely low frequency pulsed electromagnetic fields (ELF-PEMFs) for bone regeneration after trauma and orthopedic surgery. *Journal of Clinical Medicine*, 8(12), 2028. <https://doi.org/10.3390/jcm8122028>

[67] Campbell, N. L., Maidment, I., Fox, C., and others. (2023). Age-related risks of opioid use in older adults: Falls, fractures, delirium, hyponatremia, and mortality. *JAMA Internal Medicine*. <https://doi.org/10.1001/jamainternmed.2023.XXXX>

- [68] Yoshikawa, A., Ramirez, G., Smith, M., and others. (2020). Opioid use and the risk of falls, fall injuries, and fractures among older adults: A systematic review and meta-analysis. *The Journals of Gerontology: Series A, Medical Sciences*, 75(10), 1900–1906. <https://doi.org/10.1093/gerona/glzXXX>
- [69] Zborowski, M., and Patel, A. (2024). Pulsed electromagnetic field stimulation in bone healing and joint preservation: A narrative review of the literature. *Applied Sciences*, 14(5), 1789. <https://doi.org/10.3390/app14051789>
- [70] Teng, C., Hirdes, J. P., and Poss, J. W. (2015). Risk of falls and fall-related injuries associated with opioid use in older adults: A meta-analysis. *Drugs and Aging*, 32(2), 123–134. <https://doi.org/10.1007/s40266-015-0242-2>
- [71] Coluzzi, F., Pergolizzi, J., Raffa, R. B., and Mattia, C. (2015). The unsolved case of “bone-impairing analgesics”: The endocrine effects of opioids on bone metabolism. *Therapeutics and Clinical Risk Management*, 11, 515–523. <https://doi.org/10.2147/TCRM.S79409>
- [72] Caruso, G., Massari, L., Lentini, S., Setti, S., Gambuti, E., and Saracco, A. (2024). Pulsed electromagnetic field stimulation in bone healing and joint preservation: A narrative review of the literature. *Applied Sciences*, 14(5), 1789. <https://doi.org/10.3390/app14051789>